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Ultrasensitive detection of inhaled organic aerosol particles by accelerator mass spectrometry

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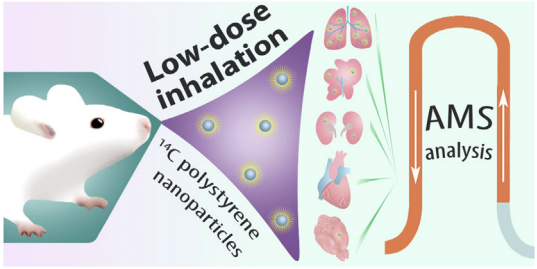
HIGHLIGHTS

- Radiocarbon labeled styrene was synthesized in five stages from ^{14}C-methanol.
- PS beads 225 ± 25 nm in size containing radiocarbon ^{14}C label were used as a model system for organic aerosol.
- Low-concentrated 10^{-3} cm^{-3} ^{14}C-aerosol was inhaled by mice during 5 days 30 min a day.
- The isotope analysis of biological probes was conducted by accelerator mass-spectrometry.
- The particle matter was directly registered in mice lungs, liver, kidneys and brain.

GRAPHICAL ABSTRACT



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ABSTRACT

Accelerator mass spectrometry (AMS) was shown to be applicable for studying the penetration of organic aerosols, inhaled by laboratory mice at ultra-low concentration ca. 10^3 cm^{-3}. We synthesized polystyrene (PS) beads, composed of radiocarbon-labeled styrene, for testing them as model organic aerosols. As a source of radiocarbon we used methyl alcohol with radioactivity. Radiolabeled polystyrene beads were obtained by emulsifier-free emulsion polymerization of synthesized ^{14}C-styrene initiated by $K_2S_2O_8$ in aqueous media. Aerosol particles were produced by pneumatic spraying of diluted ^{14}C-PS latex. Mice inhaled ^{14}C-PS aerosol consisting of the mix of 10^3 225-nm particles per 1 cm^3 and $5 \cdot 10^3$ 25-nm particles per 1 cm^3 for 30 min every day during five days. Several millions of 225-nm particles deposited in the

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Polystyrene beads
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lungs and slowly excreted from them during two weeks of postexposure. Penetration of particles matter was also observed for liver, kidneys and brain, but not for a heart.

1. Introduction

Human exposure to particulate matter (PM) has increased dramatically over the last century due to anthropogenic impact, including sharply grown combustion of fuels, developing road industry as well as thriving nanotechnologies (Oberdörster et al., 2005). A significant positive association between morbidity and nonaccidental mortality and air pollution by ultrafine(<0.1 μm in diameter), fine (from 0.1 to 2.5 μm) and course (more than 2.5 μm) particles has been indicated by many representative reports (Oberdörster et al., 2005; Pope et al., 1992; Dockery et al., 1992; Samet et al., 2000; Künzli et al., 2000; Peters et al., 1997a; Pope and Dockery, 2006). Such air pollutant as PM is believed to increase respiratory symptoms and illness, asthma exacerbations and chronic lung and heart disease (Bascom et al., 1996). PM is estimated to kill more than 500,000 people each year (Nel, 2005) or even more with predominant burden occurring in developing Asian countries (Cohen et al., 2005). The situation concerns not only adults but also children (Pope et al., 1992; Nel, 2005; Dockery et al., 1989), effected by both outdoor and indoor air (Jones, 1999; Wallace, 1996).

It has been shown that when inhaled, specific sizes of nanoparticles are deposited by three basic mechanisms: inertial impaction, sedimentation and diffusion, in all regions of the respiratory tract but with different efficiency. Less than 20% of fine particles and up to 90% of ultrafine particles deposit in the respiratory tract (Oberdörster, 2001a; Khorasanizade et al., 2011; Williams et al., 2011). After the deposition the alveolar-airway barrier allows passage of particles up to nearly 800 nm in diameter (Conhaim et al., 1988). Ultrafine particles are primarily consumed by interstitial macrophages (Donaldson et al., 1998) and unphagocytosed particles penetrate across epithelial and endothelial cells to the blood and lymph circulation and reach bone marrow, lymph nodes, spleen, and heart (Oberdörster et al., 2005; Oberdörster, 2001a). Access to the central nervous system and ganglia via translocation along of neurons has also been observed (Oberdörster et al., 2005). Ultrafine particles and, to a lesser extent, fine particles, localize in mitochondria, where they induce major structural damage, contributing to oxidative stress (Li et al., 2003).

Despite substantial findings regarding PM exposure-response function there are some important gaps and skepticism regarding “what we may think we know about the health effects of PM exposure”. (Pope and Dockery, 2006; Lumley and Sheppard, 2003). On the other hand, reliable studies on particle deposition in the respiratory tract and further particle translocation are of great value, not only to risk assessment of inhalation toxicology but also to improve efficiency in drug delivery of inhalation therapies (Williams et al., 2011; Miller et al., 1979). The problem of investigations on health effects of PM exposure is resulted from three main features of PM.

The first one is that health impacts from PM exposure with different particle size are unequal. Particles with different sizes from nm to μm represent separate classes of pollutants and have been recommended to be measured separately in aerosol research and medical studies (Wilson and Suh, 1997; Schwartz et al., 1996; Peters et al., 1997b). The second feature is low particle concentration of ambient aerosol. The relationship between air PM pollution and health was clearly observed at particle concentrations <100 μg m^{-3} (Dockery et al., 1992; Pope and Dockery, 2006), an excess risk of death of 0.5% per each 10 μg m^{-3} of PM_{10} (<10 μm in diameter) being observed from 5 to 220 μg m^{-3} (Schwartz, 1994; Brunekreef and Holgate, 2002). According to the U.S. Environmental Protection Agency, the 24-h and annual standards for $PM_{2.5}$ are 65 and 15 μg m^{-3}, respectively, and for PM_{10} they are 150 and 50 μg m^{-3}, respectively. (Ware, 2000; Bernstein et al., 2004). What is more, the levels of ultrafine particles in urban air are generally between 0.8 and 2 μg m^{-3}, or $1–5{\cdot}10^4$ cm^{-3} and only during episodic increases mass concentrations can rise to 20–50 μg m^{-3} with number concentrations rising to levels of $0.3–1{\cdot}10^6$ cm^{-3}. (Conhaim et al., 1988; Oberdörster, 2001a; Oberdörster et al., 2002a). Unlike direct measurement of PM concentration in air which is carried out with sufficient accuracy, the particle content in the tissues and organs after inhalation under the ambient conditions is extremely complicated. The third feature of PM is the predominantly organic nature of particles, mainly derived from mobile and stationary combustion processes. The smaller the particle size, the greater portion of particles consisting of organic substances, particles less than 200 nm in diameter being almost completely composed of organics (Mauderly and Chow, 2008). It should be noted that organic speciation of carboneous compounds in air, including PM constituents, presents a range of water-soluble (humic-like substances, polyols, polyethers, mono- and dicarboxylic acids etc.) and water-insoluble organic carbon (n-alkanes, n is from 14 to 42, n-alkanoic acids, polycyclic aromatic hydrocarbons, soot etc.), the last one often giving the higher contribution (Mauderly and Chow, 2008).

PM characteristics described above, namely ultra-small size, ultra-low concentrations and carboneous content of the aerosol have made direct detection of particles inhaled under natural conditions impossible to date. Due to strong analytical limitations the majority of PM health effect investigations are based on techniques that use intratracheal instillation instead of inhalation, and even when inhalation takes place, PM concentrations are much greater than 100 μg m^{-3} (Table 1) (Glover et al., 2008; Nemmar et al., 2001, 2002a; Takenaka et al., 2001; Oberdörster, 2001b; Ferin et al., 1992; Oberdorster et al., 1994; Geiser et al., 2005; Oberdörster et al., 2002b, 2004, 1992; Simon et al., 1995a; Simon et al., 1995b; Ercan et al., 1991; Gibaud et al., 1996; Nemmar et al., 2002b, 2003; Hamoir et al., 2003; Silva et al., 2005; Kato et al., 2003; Gibaud et al., 1994, 1998). In Table 1 we tried to summarize available data on the detection studies of model aerosols in living organisms showing the main problems of particle detection which force the researchers to use high particle doses or inadequate injection routes.

In order to detect particles directly in organs after inhalation, e.g. by elemental analyses, investigators have to use inorganic particle matter, such as Pt (Oberdörster, 2001a), Ag (Takenaka et al., 2001), and TiO_2 (Geiser et al., 2005) or radioactive labels, e.g. ^{99m}Tc (Glover et al., 2008; Nemmar et al., 2001, 2002a), physically attached to the particles (Table 1). In addition to inorganic matter, which differs from the ambient aerosol constituents, it cannot be excluded that in vivo dissolution and transport of the dissolved metals and labels were significant factors during particle detection (Oberdörster et al., 2002a). Another difficulty is a great dose of